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Sequence Listing was accepted.

If you need help call the Patent Electronic Business Center at (866) 217-9197 (toll free).

Reviewer: Durreshwar Anjum

Timestamp: Thu May 24 09:12:10 EDT 2007

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## Validated By CRFValidator v 1.0.2

Application No: 09618380 Version No: 7.0

Input Set:

Output Set:

**Started:** 2007-05-23 15:03:34.322 **Finished:** 2007-05-23 15:03:35.162

Elapsed: 0 hr(s) 0 min(s) 0 sec(s) 840 ms

Total Warnings: 10

Actual SeqID Count: 14

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## SUBSTITUTE SEQUENCE LISTING

<110> Weiner, George Gingrich, Roger Link, Brian Tso, J. Yun <120> HUMANIZED ANTIBODIES AGAINST CD3 <130> 011823-004920US <140> 09618380 <141> 2000-07-18 <150> US 09/618,380 <151> 2000-07-18 <150> US 08/397,411 <151> 1995-03-01 <150> US 07/859,583 <151> 1992-03-27 <160> 14 <170> PatentIn version 3.1 <210> 1 <211> 107 <212> PRT

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<223> Light chain of Humanized 1D10 Ab minus signal sequence

<400> 1

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Glu Asn Ile Tyr Ser Tyr 20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Val 35 40 45

Ser Asn Ala Lys Thr Leu Ala Glu Gly Val Pro Ser Arg Phe Ser Gly 50 55 60

Ser Gly Ser Gly Lys Gln Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro 65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln His His Tyr Gly Asn Ser Tyr 85 90 95

Pro Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys  $100 \hspace{1.5cm} \hbox{105}$ 

<210> 2

<211> 107

<212> PRT

<213> Mus sp.

<400> 2

Asp Ile Gln Met Thr Gln Ser Pro Ala Ser Leu Ser Ala Ser Val Gly

1 10 15

Glu Thr Val Thr Ile Thr Cys Arg Ala Ser Glu Asn Ile Tyr Ser Tyr
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Gln Gly Lys Ser Pro Gln Leu Leu Val 35 40 45 Ser Asn Ala Lys Thr Leu Ala Glu Gly Val Thr Ser Arg Phe Ser Gly 50 55 60 Ser Gly Ser Gly Lys Gln Phe Ser Leu Lys Ile Asn Ser Leu Gln Pro 70 75 80 Glu Asp Phe Gly Asn Tyr Tyr Cys Gln His His Tyr Gly Asn Ser Tyr 90 Pro Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys 100 105 <210> 3 <211> 116 <212> PRT <213> Artificial Sequence <220> <223> Heavy chain of Humanized 1D10 Ab minus signal sequence <400> 3 Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu 1 5 10 15 Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Thr Asn Tyr 20 25 30 Gly Val His Trp Val Arg Gln Ser Pro Gly Lys Gly Leu Glu Trp Ile 35 40 45 Gly Val Lys Trp Ser Gly Gly Ser Thr Glu Tyr Asn Ala Ala Phe Ile 50 55 Ser Arg Leu Thr Ile Ser Lys Asp Thr Ser Lys Asn Gln Val Ser Leu 65 70 75 80

Lys Leu Asn Ser Leu Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala

Arg Asn Asp Arg Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu Val 100 105 110

Thr Val Ser Ser 115

<210> 4

<211> 116

<212> PRT

<213> Mus sp.

<400> 4

Gln Val Gln Leu Lys Gln Ser Gly Pro Gly Leu Val Gln Pro Ser Gln 1 5 10 15

Ser Leu Ser Ile Thr Cys Thr Gly Ser Gly Phe Ser Leu Thr Asn Tyr 20 25 30

Gly Val His Trp Val Arg Gln Ser Pro Gly Lys Gly Leu Glu Trp Leu 35 40 45

Gly Val Lys Trp Ser Gly Gly Ser Thr Glu Tyr Asn Ala Ala Phe Ile 50 55 60

Ser Arg Leu Ser Ile Ser Lys Asp Asn Ser Lys Ser Gln Val Phe Phe 65 70 75 80

Lys Met Asn Ser Leu Gln Ala Asp Asp Thr Ala Met Tyr Tyr Cys Ala 85 90 95

Arg Asn Asp Arg Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Ser Val $100 \hspace{1.5cm} 105 \hspace{1.5cm} 110$ 

Thr Val Ser Ser 115

<210> 5

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<211> 214
<212> PRT
<213> Artificial Sequence
<220>
<223> Complete light chain of Humanized 1D10 Ab
<400> 5
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Glu Asn Ile Tyr Ser Tyr
      20 25
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Val
   35
            40
Ser Asn Ala Lys Thr Leu Ala Glu Gly Val Pro Ser Arg Phe Ser Gly
  50 55 60
Ser Gly Ser Gly Lys Gln Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
            70
                     75
65
Glu Asp Phe Ala Thr Tyr Tyr Cys Gln His His Tyr Gly Asn Ser Tyr
         Pro Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala
     100 105 110
Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
   115 120 125
Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
         135
 130
Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
                     155
145
         150
Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
```

165 170 175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr 180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser 195 200 205

Phe Asn Arg Gly Glu Cys 210

<210> 6

<211> 273

<212> PRT

<213> Artificial Sequence

<220>

<223> Fd-jun in F(ab'-zipper)2 of humanized 1D10 antibody

<400> 6

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu  $1 \hspace{1.5cm} 5 \hspace{1.5cm} 10 \hspace{1.5cm} 15$ 

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Thr Asn Tyr 20 25 30

Gly Val His Trp Val Arg Gln Ser Pro Gly Lys Gly Leu Glu Trp Ile 35 40 45

Gly Val Lys Trp Ser Gly Gly Ser Thr Glu Tyr Asn Ala Ala Phe Ile 50 55 60

Ser Arg Leu Thr Ile Ser Lys Asp Thr Ser Lys Asn Gln Val Ser Leu 65 70 75 80

Lys Leu Asn Ser Leu Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala 85 90 95

Arg Asn Asp Arg Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala 115 120 125 Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu 130 135 140 Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly 145 150 155 160 Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser 165 170 Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu 180 185 190 Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr 200 205 195 Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr 210 215 220 Cys Pro Pro Cys Lys Cys Pro Ala Gly Gly Arg Ile Ala Arg Leu Glu 225 230 235 240 Glu Lys Val Lys Thr Leu Lys Ala Gln Asn Ser Glu Leu Ala Ser Thr 245 250 255 Ala Asn Met Leu Arg Glu Gln Val Ala Gln Leu Lys Gln Lys Val Met 260 265 270 Asn <210> 7 <211> 446

<220>

<212> PRT

<213> Artificial Sequence

<223> Complete heavy chain of Humanized 1D10 Ab

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Thr Asn Tyr 20 25 30

Gly Val His Trp Val Arg Gln Ser Pro Gly Lys Gly Leu Glu Trp Ile \$35\$

Gly Val Lys Trp Ser Gly Gly Ser Thr Glu Tyr Asn Ala Ala Phe Ile 50 55 60

Ser Arg Leu Thr Ile Ser Lys Asp Thr Ser Lys Asn Gln Val Ser Leu 65 70 75 80

Lys Leu Asn Ser Leu Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala 85 90 95

Arg Asn Asp Arg Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu Val 100 105 110

Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala 115 120 125

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu 130 135 140

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser 165 170 175

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu 180 185 190

Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr 195 200 205

Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr 210 215 220

Суз 225	Pro	Pro	Суз	Pro	Ala 230	Pro	Glu	Leu	Leu	Gly 235	Gly	Pro	Ser	Val	Phe 240
Leu	Phe	Pro	Pro	Lys 245	Pro	Lys	Asp	Thr	Leu 250	Met	Ile	Ser	Arg	Thr 255	Pro
Glu	Val	Thr	Суз 260	Val	Val	Val	Asp	Val 265	Ser	His	Glu	Asp	Pro 270	Glu	Val
Lys	Phe	Asn 275	Trp	Tyr	Val	Asp	Gly 280	Val	Glu	Val	His	Asn 285	Ala	Lys	Thr
Lys	Pro 290	Arg	Glu	Glu	Gln	Tyr 295	Asn	Ser	Thr	Tyr	Arg 300	Val	Val	Ser	Val
Leu 305	Thr	Val	Leu	His	Gln 310	Asp	Trp	Leu	Asn	Gly 315	Lys	Glu	Tyr	Lys	Cys 320
Lys	Val	Ser	Asn	Lys 325	Ala	Leu	Pro	Ala	Pro 330	Ile	Glu	Lys	Thr	Ile 335	Ser
Lys	Ala	Lys	Gly 340	Gln	Pro	Arg	Glu	Pro 345	Gln	Val	Tyr	Thr	Leu 350	Pro	Pro
Ser	Arg	Asp 355	Glu	Leu	Thr	Lys	Asn 360	Gln	Val	Ser	Leu	Thr 365	Cys	Leu	Val
Lys	Gly 370	Phe	Tyr	Pro	Ser	Asp 375	Ile	Ala	Val	Glu	Trp 380	Glu	Ser	Asn	Gly
Gln 385	Pro	Glu	Asn	Asn	Tyr 390	Lys	Thr	Thr	Pro	Pro 395	Val	Leu	Asp	Ser	Asp 400
Gly	Ser	Phe	Phe	Leu 405	Tyr	Ser	Lys	Leu	Thr 410	Val	Asp	Lys	Ser	Arg 415	Trp
Gln	Gln	Gly	Asn 420	Val	Phe	Ser	Cys	Ser 425	Val	Met	His	Glu	Ala 430	Leu	His
Asn	His	Tyr 435	Thr	Gln	Lys	Ser	Leu 440	Ser	Leu	Ser	Pro	Gly 445	Lys		

<210> 8 <211> 106 <212> PRT <213> Artificial Sequence <220> <223> Light chain of Humanized M291 Ab minus signal sequence <400> 8 Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly 10 15 Asp Arg Val Thr Ile Thr Cys Ser Ala Ser Ser Ser Val Ser Tyr Met 20 25 30 Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Leu Ile Tyr 35 40 45 Asp Thr Ser Lys Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser 50 55 60 Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu 65 70 75 Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Pro Thr 85 90 95 Phe Gly Gly Gly Thr Lys Val Glu Ile Lys 100 105 <210> 9 <211> 106

<213> Mus sp.

<212> PRT

Gln Ile Val Leu Thr Gln Ser Pro Ala Ile Met Ser Ala Ser Pro Gly 1 5 10 15 Glu Lys Val Thr Met Thr Cys Ser Ala Ser Ser Ser Val Ser Tyr Met 20 25 Asn Trp Tyr Lys Gln Lys Ser Gly Thr Ser Pro Lys Arg Trp Thr Tyr 35 40 Asp Thr Ser Lys Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser 55 Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Ser Met Glu Ala Glu 
 65
 70
 75
 80
 Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Pro Thr 90 85 Phe Gly Ser Gly Thr Lys Leu Glu Ile Lys 100 105 <210> 10 <211> 120 <212> PRT <213> Artificial Sequence <220> <223> Heavy chain of Humanized M291 Ab minus signal sequence <400> 10 Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Ile Ser Tyr 20 25 30 Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met 35 40 45

Gly Tyr Ile Asn Pro Arg Ser Gly Tyr Thr His Tyr Asn Gln Lys Leu

50 55 60

Lys Asp Lys Ala Thr Leu Thr Ala Asp Lys Ser Ala Ser Thr Ala Tyr 65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys 85 90 95

Ala Arg Ser Ala Tyr Tyr Asp Tyr Asp Gly Phe Ala Tyr Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser 115 120

<210> 11

<211> 120

<212> PRT

<213> Mus sp.

<400> 11

Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Ala Arg Pro Gly Ala 1  $\phantom{\bigg|}$  5  $\phantom{\bigg|}$  10  $\phantom{\bigg|}$  15

Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe Ile Ser Tyr 20 25 30

Thr Met His Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile \$35\$ 40 45

Gly Tyr Ile Asn Pro Arg Ser Gly Tyr Thr His Tyr Asn Gln Lys Leu 50 55 60

Lys Asp Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Ser Ala Tyr 65 70 75 80

Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys 85 90 95

Ala Arg Ser Ala Tyr Tyr Asp Tyr Asp Gly Phe Ala Tyr Trp Gly Gln 100 105 110

Gly Thr Leu Val Thr Val Ser Ala 115 120

<210> 12

<211> 213

<212> PRT

<213> Artificial Sequence

<220>

<223> Complete light chain of Humanized M291 Ab

<400> 12

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly

1 10 15

Asp Arg Val Thr Ile Thr Cys Ser Ala Ser Ser Ser Val Ser Tyr Met 20 25 30

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg